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RACE INTERACTIONS AND FOOT FUNCTION IN OLDER ADULTS: THE JOHNSTON COUNTY OSTEOARTHRITIS PROJECT

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Purpose: Center of pressure excursion index (CPEI), a measure that characterizes pronation and supination, may be a useful indicator of foot function. Data from the predominantly Caucasian Framingham Foot Study have shown that CPEI differed significantly by age and sex. The purpose of this study was to examine whether demographic and clinical traits were associated with CPEI in a large bi-racial cohort of men and women ≥ 50 years of age.
Methods: Of the 1695 Johnston County Osteoarthritis Project participants clinically evaluated in 2006-2010, 1466 were enrolled in a comprehensive foot study. As part of the exam, participants were instructed to walk at a self-selected pace over a Tekscan Matscan system (Tekscan, Inc., Boston) using the two-step method. Two plantar pressure scans were recorded for each foot. Custom software was used to calculate CPEI and was averaged for each foot; the foot with the averaged CPEI value farthest from the median was used in analyses. A higher CPEI value indicates a more supinated foot, while lower CPEI indicates a more pronated foot. Characteristics included sex, age (< 65 or ≥ 65 years), body mass index (BMI, <30 or ≥ 30 kg/m^2), and race (Caucasian or African-American). Student's t-test was used to identify those factors associated with differences in mean CPEI for the sample and stratified by sex. Linear regression was used to evaluate interactions of continuous factors (age and BMI) by race.
Results: Participants (67% women, 29% African-American) had mean age of 68 years and mean BMI of 31 kg/m^2. The mean CPEI was smaller among women than men (p<0.0001, Table). In the total sample, CPEI differed by age group with participants 65+ yrs having lower CPEI (p<0.0001), indicating a tendency toward more pronation with age. When this difference was stratified by sex (Table), women 65+ yrs continued to have lower CPEI (p=0.0002); men had a similar result albeit with borderline statistical significance (p=0.07). CPEI did not differ by BMI or by race. However, significant interactions were noted between race and continuous age (p=0.022), as well as between race and continuous BMI (p=0.026), with CPEI in women only. While older women of either race had lower CPEI (as did those with higher BMI), the difference was twice as large in African-American (~3.2 CPEI units, p=0.002) than Caucasian women (~1.5 units, p=0.02).
Conclusions: Similar to results reported in the Caucasian Framingham Foot Study, we found significant differences in mean CPEI that indicate over-pronation for those aged 65+ yrs and for women, but found no link between CPEI and BMI. While there was no main effect by race for the categorical data, the interactions in women by race imply that there may be a greater age effect towards pronation in older African-American women. This might indicate more foot pathology, an underlying genetic component of foot function or perhaps even more need for treatment of the pronated foot in this group.

Table
T-tests for associations between demographic and clinical variables and CPEI in men and women

Males	N	Mean CPEI	Standard Deviation	p	Females	N	Mean CPEI	Standard Deviation	p
Sex	481	16.3	8.4		Sex	985	14.4	8.8	<.0001
Age < 65	214	17.1	8.8	0.07	Age < 65	384	15.7	8.5	0.0002
Age ≥ 65	267	15.7	7.9		Age ≥ 65	601	13.6	8.9	
BMI < 30	241	16.4	8.6	0.78	BMI < 30	477	14.0	9.1	0.13
BMI ≥ 30	240	16.2	8.1		BMI ≥ 30	508	14.8	8.4	
Caucasian	363	16.6	8.2	0.13	Caucasian	671	14.4	8.7	0.72
African-Am	118	15.3	8.8		African-Am	314	14.6	9.1	

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THE ACTIVATED PATIENT INFLUENCES PRIMARY CARE PHYSICIANS' PRESCRIPTIONS OF CELEBREX FOR OSTEOARTHRITIS

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Purpose: Direct to consumer marketing of medications is intended to "activate" patients to request the advertised medication from their physicians. There is limited data on the extent to which physicians alter prescribing patterns in response to specific requests from activated patients.
Methods: We performed a factorial experiment in which primary care physicians viewed clinically authentic videotapes of "patients" presenting with symptomatic knee osteoarthritis (OA). The "patients" were played by professional actors who differed by sex, race (white, Black, Hispanic) and SES (higher, lower). 192 primary care physicians working primarily in Illinois were recruited to participate. Each physician viewed one vignette of a patient with typical symptoms of knee OA lasting for several months. In one half of vignettes the patient was 'activated' and asked: *"I've seen ads for Celebrex and it looks just like what I need···A woman I work with takes it and she said it really works for her···so, I really want to try that."* The non activated patients requested help with their pain but did not ask for any specific medications*: "I just want something to make it better."* Activated and nonactivated vignettes were balanced on sex, race and SES. Physicians were balanced by sex and years of experience. After viewing the videotape, the physicians completed a questionnaire in which they indicated the treatment(s) they would likely order. We examined the association between patient characteristics, particularly activated vs. non-activated, and the medications the physicians said they would prescribe (celecoxib, non-selective NSAIDs, other) using a multivariate ANOVA model.
Results: 53% of the PCPs presented with a vignette including an active request for celecoxib reported that they would prescribe celecoxib, as compared with 24% of physicians seeing the identical vignette without an active medication request (p<0.0001; Table). Physicians receiving an active request for celecoxib were less likely to report that they would prescribe a non-selective NSAID (29%) than physicians whose simulated patients did not request celecoxib (42%; p=0.06). Further, physicians who received an active request for celecoxib prescribed either a COX-2 OR a traditional NSAID for 82% of vignettes, compared to 66% of physicians who did not receive an active request (p=0.004). The associations between active request and physician prescribing patterns were not influenced by patient characteristics (gender, race, SES) or physician characteristics (gender, experience).
Conclusions: Physicians presented with an activated request for celecoxib by a patient with typical knee OA were more than twice as likely to prescribe celecoxib compared to physicians encountering a non-activated patient who provided the same clinical history and they were also considerably more likely to prescribe *any* NSAID (selective or non-selective) . Given the higher price, increased risk of cardiovascular toxicity and similar efficacy of celecoxib compared to non-selective NSAIDs, these findings suggest that patient activation may increase health care costs and compromise appropriateness of prescribing.

Table
Prescription of celecoxib and other NSAIDs for OA: Stratified by active patient request

Active Request	Celecoxib	NSAID, not Cox-2	Celecoxib *OR* non-selective	Neither
Yes	51 (53%)	28 (29%)	79 (82%)	17 (18%)
No	23 (24%)	40 (42%)	63 (66%)	33 (34%)

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VITAMIN K STATUS AND MRI-BASED KNEE OSTEOARTHRITIS CHARACTERISTICS IN COMMUNITY-DWELLING OLDER ADULTS: THE HEALTH ABC STUDY

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Several vitamin K dependent proteins are present in joint tissues, including matrix gla protein (MGP) which functions as a calcification inhibitor. In order for MGP to function it must be γ-carboxylated, which requires vitamin K. Ex vivo studies suggest MGP carboxylation is relevant to osteoarthritis (OA). Assays that measure uncarboxylated MGP (ucMGP) in plasma have been developed, and elevated plasma ucMGP reflects lower vitamin K status. Whether or not plasma ucMGP is associated with OA is unclear.

Purpose: To determine the association between plasma ucMGP and vitamin K1 and knee OA features assessed using MRI in the Health Aging and Body Composition (Health ABC) study of well-functioning community-dwelling older adults.

Methods: 437 participants with qualifying knee pain and 144 randomly chosen controls underwent bilateral knee MRIs (mean±SD age = 74±3 yr; 66% female). Using the WORMS method, the anterior, central, and posterior of the medial/lateral femoral condyles/tibial plateaus and medial/lateral subregions of the patella were each semi-quantitatively scored separately for cartilage damage, bone marrow lesions, subarticular cysts, osteophytes, and bone attrition. Meniscal damage was scored separately in medial and lateral compartments and synovitis was assessed in the whole knee. Vitamin K status was measured according to plasma ucMGP and vitamin K1 concentrations. Using the knee as the unit of analysis, the ORs (95%CIs) for presence of OA characteristics were calculated using logistic regression with generalized estimating equations (GEEs, to account for between-knee correlation), according to quartile of each vitamin K status measure. Linear regression with GEEs was used to compare the scores for each knee OA feature across vitamin K status quartiles. Adjustment was made for age, gender, race, BMI, smoking status, interleukin-6, and education.

Results: Those with lower plasma ucMGP (reflective of better vitamin K status) were significantly less likely to have any bone marrow lesions [OR(95%CI) comparing lowest to highest quartile: 0.59(0.39-0.91), p-trend=0.01] and osteophytes [OR(95%CI)=0.55(0.37-0.84), p-trend=0.004]. There was a borderline trend for a lower prevalence of meniscal damage [OR(95%CI)=0.68(0.44-1.04), p-trend=0.049] and subarticular cysts [OR(95%CI)=0.75(0.50-1.14), p-trend=0.07]. In the linear models, plasma ucMGP was significantly positively associated with total bone marrow lesion score (beta coefficient=0.085; p=0.003) and total subarticular cyst score (beta coefficient=0.071; p=0.003). Plasma ucMGP was not associated with cartilage damage ($p \geq 0.16$), bone attrition ($p \geq 0.53$), or synovitis ($p \geq 0.90$) and plasma vitamin K1 was not associated with any MRI knee OA feature (all $p \geq 0.22$).

Conclusion: In this cross-sectional analysis, a marker of lower vitamin K status, plasma ucMGP, but not vitamin K1 itself was associated with some knee OA MRI features, especially those related to subchondral bone. Longitudinal analyses are needed to determine whether either plasma ucMGP or vitamin K1, predict changes in knee OA features.

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CIGARETTE SMOKING AND RISK OF SEVERE OSTEOARTHRITIS AMONG CHINESE IN SINGAPORE - THE SINGAPORE CHINESE HEALTH STUDY

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Purpose: Although cigarette smoking has been associated with a protective effect for osteoarthritis (OA) in several Western studies, results are conflicting and none has examined the effect of smoking cessation. There is also no data from Asian countries where the prevalence of knee OA is increasing. We aimed to examine smoking status, duration, dosage and cessation in relation to the risk of total knee replacement (TKR) for severe knee OA among elderly Chinese in Singapore.

Methods: We used data from the Singapore Chinese Health Study, a population-based prospective cohort of 63,257 Chinese men and women aged 45 to 74 years at enrolment between 1993 and 1998. Detailed information on smoking, current diet, medical history and lifestyle factors were obtained through in-person interviews at enrollment. The cohort has been continuously followed, both actively through re-interviews and passively through computer linkage to population-based death and cancer registries. Loss to follow-up has been negligible. As of 31 December 2011, after a mean follow-up of 14.5 years, 1,950 incident TKR cases for severe knee OA (324 cases in men and 1,626 cases in women) were identified via linkage with nationwide hospital discharge database. We used the Cox regression models to examine smoking in relation to risk of TKR with adjustment for age at and year of study enrollment, level of education, body mass index and physical activity level.

Results: Compared to never smokers, current smokers had a statistically significant 51% decrease in risk of TKR [hazards ratio (HR)=0.49; 95% confidence interval (CI)=0.40-0.60], while former smokers had a 15% reduction in risk (HR=0.85; 95% CI=0.69-1.04). The risk estimates were similar between both genders. Among current smokers, there was a very strong dose-dependent association between increasing duration of smoking and decreasing risk of TKR. Compared to never smokers, the relative risk decreased from 0.81 (95% CI=0.47-1.39) in the current smokers who had smoked less than 20 years to 0.36 (95% CI=0.26-0.50) in those who had smoked for 40 or more years (p for trend<0.0001). A strong negative linear effect of smoking intensity was also detected with the relative risk decreasing from 0.55 (95% CI=0.43-0.71) in current smokers who smoked fewer than 13 cigarettes per day to 0.33 (95% CI=0.14-0.80) in those who smoked at least 33 cigarettes per day (p for trend<0.0001), when compared to never smokers. Among former smokers, there was a stepwise dose-dependent attenuation in the risk reduction of TKR with duration of cessation. Compared to never smokers, the relative risk of TKR was 0.68 among those who had quit less than 1 year, and increased to 0.98 in those who had quit for at least 20 years (p for trend<0.0001).

Conclusions: Our findings strongly implicate cigarette smoking as a protective factor for severe osteoarthritis, and this protection is rapidly lost with smoking cessation. This concurs with experimental data that nicotine promotes proliferation and collagen synthesis in chondrocytes. While we certainly do not advocate smoking as a means of preventing onset or progression of osteoarthritis, understanding the role of nicotine will elucidate pathogenesis of OA and help in the development of chemopreventive agents targeting this putative pathway.

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SYMPTOMATIC HAND OSTEOARTHRITIS (OA) AND THE ASSOCIATIONS TO MORTALITY AND CARDIOVASCULAR EVENTS - DATA FROM THE FRAMINGHAM OA STUDY

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Purpose: To study whether participants with symptomatic hand OA had increased mortality and more cardiovascular events in a population-based cohort, and to explore mechanisms behind a potential association.

Methods: We included participants from the Framingham Original and Offspring cohorts between 50 and 75 years, without rheumatoid arthritis and with available hand radiographs and/or information about hand pain enabling classification of symptomatic hand OA. Symptomatic hand OA was defined as one or more hand joint(s) with radiographic OA (Kellgren Lawrence grade 2 or more) and pain in the same joint(s). Overall mortality included mortality related to cardiovascular events, cancer and mortality due to unknown/unspecified causes. For cardiovascular events, we focused on incident coronary heart disease (coronary insufficiency/myocardial infarction), congestive heart failure and/or atherothrombotic brain infarction. The diagnoses were arrived at by a panel of cardiologists/neurologists using published criteria after review of clinical examinations and hospitalization records. As covariates we included body mass index (BMI), blood glucose, lipid profile, blood pressure, medication use (lipid-lowering, antihypertensive, antidiabetics, nonsteroidal anti-inflammatory drugs and aspirin), smoking and alcohol (for mortality: also previous cardiovascular events and cancer). The associations to cardiovascular events were studied in those with no previous events. We examined whether symptomatic hand OA was associated with all-cause mortality and cardiovascular events using Cox proportional hazards models adjusting for age, sex, cohort and BMI (adjusted model one), as well as other covariates at baseline (adjusted model two).